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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,724	12/08/2003	Antonius Arnoldus Christiaan Jacobs	I 1999.452 US C1	5481

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,724	JACOBS ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/08/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 12/08/03 has been acknowledged.

Claims 1-5 are canceled.

Claims 6-11 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No.

6,682,745. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of invention as claimed in the instant application (any bacterial vaccine) encompasses the invention claimed in the US '745 (*Streptococcus equi and Streptococcus zooepidemicus)*.

The scope of the invention as claimed in the instant application encompasses a method of administering a live attenuated bacterial vaccine (any bacteria) to a mammal by injecting the vaccine into submucosal layer of a mammal and a method for reducing the amount of adverse reaction in the injected mammal at the injection site. The scope of the invention claimed in the US '745 encompasses a method of administering a live attenuated *Streptococcus equi and Streptococcus zooepidemicus* bacterial vaccine to a mammal by injecting the vaccine into submucosal layer of a mammal and a method for reducing the amount of adverse reaction in the injected mammal at the injection site.

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of instant application by substituting the *Streptococcus equi and Streptococcus zooepidemicus* with other live attenuated bacterial strains selected from a group consisting of *Actinobacillus equili, A. pleuropneumoniae, Actinomyces pyoyenes, Botdetella bronchiseptica, Brucella abortus, Clostridium perfringens, Corynebacterium bovis, C pseudotuberculosis, Erysipelotrix rhusioipathiae, Escherichia coli, Haemophilus parasuis, Leptospira canicola, L. hardjo, L icterohaemorrhagiae, L. poriona, Mycobacterium bovis, Mycoplasma bovis, M. hyopneumoniae, Noccatdia asteroides, Pasteurella haemolytica, P. multocida, Pseudomonas mallei, Rhodococcus equi, Salmonella cholerasuis, S. dublin, S. typimurium, Serpulina hyodysenteriae, Staphylococcus aureus, Streptococcus agalactiae, St. pneumoniae, St.suis, or St. uberi.* One would have been motivated to do so induce host immune response against the live attenuated bacterial strain of choice without any adverse reaction. One would have a reasonable expectation of success in doing so, since submucosal injection of a composition has been within the reach of one ordinary skilled in the art at the instant invention was made. Therefore the invention of instant application is an obvious extension of invention claimed in the US 745 patent.

Claims 6-8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,120,775 (ref.

of record). Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of invention as claimed in the instant application encompasses the invention of claim 1 of '775.

The scope of the invention as claimed in the instant application encompasses a method of administering a live attenuated bacterial vaccine (any bacteria) to a mammal by injecting the vaccine into submucosal layer of a mammal. The scope of the invention claimed in the US '775 encompasses a method of administering a live attenuated *Streptococcus equi* bacterial vaccine to a horse by administering the vaccine into submucosal layer of the horse.

Thus would have been obvious to modify the invention of US '775 by substituting submucosal or labial administration by a submucosal injecntion. One would have been motivated to do so avoid the dispersion of vaccine composition due to salivary contents in the mouth. One would have a reasonable expectation of success since administration of a vaccine by an injection device has been routine in the art at the time of filing. Therefore the invention of instant application is an obvious extension of invention claimed in the US 775 patent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of the instant invention as claimed encompasses a method of administering a live attenuated bacterial vaccine (any bacteria) to a mammal by injecting the vaccine into submucosal layer of a mammal. The scope of invention as claimed further encompasses a method for reducing the amount of adverse reaction in a mammal at injection site of live attenuated bacterial vaccine (any bacteria) by administering the vaccine submucosally. The scope of invention as claimed encompasses the use of any and all live attenuated bacteria. At best the instant specification only discloses the use of *Streptococcus equi* attenuated strains (TW 928 and TW928/sls), which are deletion mutant vaccine strains (spec. page 7, example-1). Besides TW 928 (*Streptococcus equi)* the instant specification fails to disclose any live attenuated vaccine obtained from any other bacterial strain. Especially the specification fails to disclose a live attenuated vaccine obtained from *Actinobacillus equili, A. pleuropneumoniae, Actinomyces pyoyenes, Botdetella bronchiseptica, Brucella abortus, Clostridium perfringens, Corynebacterium bovis, C pseudotuberculosis, Erysipelotrix rhusioipathiae, Escherichia coli, Haemophilus parasuis, Leptospira canicola, L. hardjo, L icterohaemorrhagiae, L. poriona, Mycobacterium bovis, Mycoplasma bovis, M. hyopneumoniae, Noccatdia asteroides, Pasteurella haemolytica, P. multocida, Pseudomonas mallei, Rhodococcus equi, Salmonella cholerasuis, S. dublin, S. typimurium, Serpulina hyodysenteriae, Staphylococcus aureus, Streptococcus agalactiae, St. pneumoniae, St.suis, or St. uberis* explicitly or implicitly as putatively considered by the applicant.

The state of the art regarding attenuated bacterial vaccine was such that a rational approach to design a live attenuated bacterial vaccine involves genetic modification of the bacterial pathogen to make the pathogen less virulent while maintaining the stability of protective antigen expression that provides immune protection. The attenuation should be an inherent property of the bacterial vaccine and not be dependent on fully functional host defenses and immune response capabilities. (Curtiss R. J. Clin. Invest. 110(8):1061-1066, 2002, ref of record). In addition, the attenuation of a bacterium requires the modification of specific bacterial genes that render the bacterial strain non-virulent. For example, inactivation of PhoP/phoq regulatory system in S. typhi results in strains, which are suitably attenuated for use as

vaccines (Tiball et al Vaccine 19:4175-4184, 20001, *ref of record*, see page 4177 sec 3.1). Even though instant specification discloses only *Streptococcus equi* based attenuated strains (TW 928 and TW928/sls) the disclosure is considered insufficient, since the specification fails to disclose how to attenuate of any other species of bacteria that can be used as a vaccine without any adverse reaction. The state of the art clearly teaches that understanding of regulatory pathways that affect bacterial virulence and protective antigens that provides long-term immune protection are consider germane to the development of a live attenuated bacterial vaccine.

Furthermore, the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case claims to live attenuated bacteria has been defined only by a statement of bacterial growth and proliferation (live attenuated) which conveyed no distinguishing information about the identity of various live attenuated bacterial species (as claimed), such as genetic modification or antigenic characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for protecting a mammal against *Streptococcus equi* infection by administering a live attenuated *Streptococcus equi* strain (TW980), does not reasonably provide enablement for a method for protecting a mammal against all bacterial infection by administering any and all live attenuated

bacterial strains. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of invention

The instant invention is drawn to live attenuated bacterial vaccine.

Breadth of Claims and Guidance Provided in the Specification

The scope of the instant invention as claimed encompasses a method of administering a live attenuated bacterial vaccine (any bacteria) to a mammal by injecting the vaccine into submucosal layer of a mammal. The scope of invention as claimed further encompasses a method for reducing the amount of adverse reaction in a mammal at injection site of live attenuated bacterial vaccine (any bacteria) by administering the vaccine submucosally. The scope of invention as claimed encompasses the use of any and all live attenuated bacteria. At best the instant specification only discloses the use of *Streptococcus equi* attenuated strains (TW 928 and TW928/sls), which are deletion mutant vaccine strains (spec. page 7, example-1). Besides TW 928 (*Streptococcus equi)* the instant specification fails to disclose any live attenuated vaccine obtained from any other bacterial strain. Especially the specification fails to disclose a live attenuated vaccine obtained from *Actinobacillus equili, A. pleuropneumoniae, Actinomyces pyoyenes, Botdetella bronchiseptica, Brucella abortus, Clostridium perfringens, Corynebacterium bovis, C pseudotuberculosis, Erysipelotrix rhusioipathiae, Escherichia coli, Haemophilus parasuis, Leptospira canicola, L. hardjo, L icterohaemorrhagiae, L. poriona, Mycobacterium bovis, Mycoplasma bovis, M. hyopneumoniae, Noccatdia asteroides, Pasteurella haemolytica, P. multocida, Pseudomonas mallei, Rhodococcus equi, Salmonella cholerasuis, S. dublin, S. typimurium, Serpulina hyodysenteriae, Staphylococcus aureus, Streptococcus agalactiae, St. pneumoniae, St.suis, or St. uberis* explicitly or implicitly as putatively claimed herein.

State of art and predictability

The state of attenuated bacterial vaccine art teaches was such that a rational approach to design a live attenuated bacterial vaccine involves genetic modification of the bacterial pathogen to make the pathogen less virulent while maintaining the stability

of protective antigen expression that provides immune protection. The attenuation should be an inherent property of the bacterial vaccine and not be dependent on fully functional host defenses and immune response capabilities. (Curtiss R. J. Clin. Invest. 110(8):1061-1066, 2002, ref. of record). In addition, the attenuation of a bacterium requires the modification of specific bacterial genes that render the bacterial strain non-virulent. For example, inactivation of PhoP/phoq regularoty system in S. typhi results in strains, which are suitably attenuated for use as vaccines (Tiball et al Vaccine 19:4175-4184, 20001, *ref of record*, see page 4177 sec 3.1). Furthermore, the development of live attenuated bacterial vaccine has not been always predictable. For example, development of a live attenuated *Shigella* vaccine that is sufficiently attenuated to be non-reactive yet adequately invasive to be highly immunogenic took 30 years in making, since it required substantial understanding of molecular genetic basis of virulence of *Shingella* (Curtiss page 1063, col.2). Although, the instant specification discloses *Streptococcus equi* based attenuated bacterial strains (TW 928 and TW928/sls), it fails to provide any guidance regarding the attenuation of any other species of bacteria. For example, the specification fails to provide any guidance regarding how to make a live attenuated bacterium selected from the above-mentioned species (see claims 7 and 11). The specification fails to disclose what are the bacterial regulatory systems in these bacteria, mutation of which would result in the making of a live attenuated bacterial strain that would provide protect a mammal against any specific bacterial infection. The state of the art clearly teaches that understanding of regulatory pathways that affect bacterial virulence and protective antigens that provides long-term immune protection are consider germane to the development of a live attenuated bacterial vaccine.

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or

exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. In instant case to practice the invention, as claimed one would require a live attenuated vaccine on hand. However the specification fails to provide any guidance regarding how make a live attenuated vaccine for all bacterial strains (other than *Streptococcus equi* attenuated strains TW928).

In addition, making any and all types of live attenuated bacterial vaccines and protecting a mammal against any and all type of bacterial infection using the live attenuated bacterial vaccines (wherein the attenuation of a specific bacterial genetic regulatory system has not been disclosed) are not considered routine in the art and without sufficient guidance to a specific bacterial strain experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988). The amount of undue experimentation required would include characterization of any and all bacterial strains (as claimed) to find out which regulatory systems could be genetically manipulated so that the attenuation renders the bacterium non-virulent while maintaining the stability of protective antigen expression that provides immune protection. In addition the undue experimentation required would further include the testing of all attenuated bacterial species in any and all mammals to evaluate of the efficacy of the live attenuated bacterial vaccine made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

Sumesh Kaushal
Examiner GAU 1636

SUMESH KAUSHAL
PATENT EXAMINER